WHAT IS CLAIMED IS:

1. A method for identifying a compound as an inhibitor of cathepsin S activity comprising the steps of

a) incubating eukaryotic host cells possessing endogenous cathepsin S activity with said compound;

b) adding a substrate to said eukaryotic host cells in the presence of said compound;

c) incubating said substrate in the presence of said compound;

d) stopping the reaction;

e) quantifying the amount of said substrate in complex with cathepsin S in said eukaryotic host cells; and

f) identifying said compound as an inhibitor of cathepsin S activity.

2. The method of Claim 1, wherein said eukaryotic host cells are peripheral human whole blood cells.

3. The method of Claim 2, wherein said incubation of said peripheral human whole blood cells with said compound occurs at a temperature between about 20° C and about 37° C.

4. The method of Claim 1, wherein said added substrate comprises a synthetic probe that forms an irreversible adduct with cathepsin S at the active site via an electrophilic functionality of said probe.

5. The method of Claim 4, wherein said electrophilic functionality of said probe comprises ketones substituted in alpha with a leaving group.

6. The method of Claim 4, wherein said probe also comprises a functional group to allow the detection of the irreversible cathepsin S-probe adduct.

7. The method of Claim 6, wherein said functional group comprises a moiety selected from the group consisting of a radioactive functional group and a non-radioactive functional group.

8. The method of Claim 7, wherein said radioactive functional group is ^{125}Iodine.

9. The method of Claim 7, wherein said non-radioactive functional group is Iodine.

10. The method of Claim 7, wherein said non-radioactive probe is used to modulate the amount of radioactivity used in said method.

11. The method of Claim 1, wherein said incubation of said substrate in the presence of said compound occurs for a period of about 30 minutes to about 3 hours, and at a temperature between about 20° C and about 37° C.

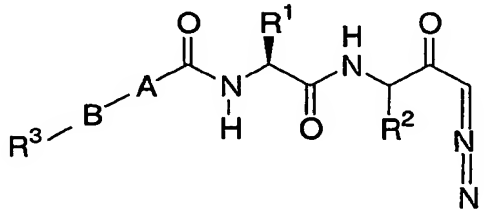
12. The method of Claim 1, wherein the reaction is stopped by the addition of an irreversible inhibitor that acts by binding to the active site cysteine residue of cathepsin S.

13. The method of Claim 12, wherein the irreversible inhibitor is N-[(1S)-1-[[[1-(2-diazoacetyl)butyl]amino]carbonyl]-3-methylbutyl]-4'-iodo-[1,1'-biphenyl]-4-carboxamide.

14. The method of Claim 12, wherein the irreversible inhibitor is E-64-D.

15. The method of Claim 1, wherein said compound is identified as an inhibitor of cathepsin S activity based on its ability to compete with said substrate for the active site of cathepsin S in said eukaryotic host cells.

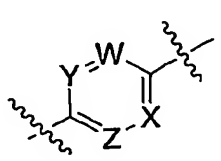
16. A compound of Formula I



I

wherein:

A and B are independently selected from



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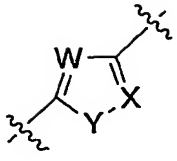

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W, X, Y and Z are independently selected from CH, S, N or O;

R^1 is selected from C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_3-C_{10} cycloalkyl, aralkyl or -$(CR^a_2)_tSO_2$-; wherein said groups are optionally substituted on the carbon or the sulfur with one to five substituents selected from halogen, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_3-C_{10} cycloalkyl, aryl or heterocyclyl;

R^2 is selected from C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_3-C_{10} cycloalkyl, aryl, aralkyl, or heterocyclyl; wherein said alkyl, alkenyl, cycloalkyl, aryl, aralkyl and heterocyclyl groups are optionally substituted with one to five substituents selected from halogen, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_3-C_{10} cycloalkyl, aryl or heterocyclyl;

R^3 is selected from ^{125}Iodine and Iodine;

Each R^a is independently selected from hydrogen and C_1-C_3 alkyl;

t is 0 to 3;

or a pharmaceutically acceptable salt or stereoisomer thereof.

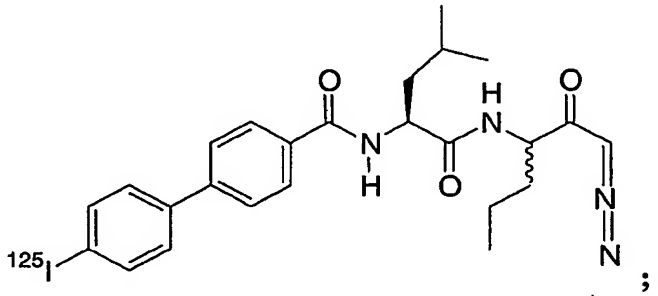
17. The compound according to Claim 16, wherein

R^1 is selected from C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, or aralkyl; wherein said alkyl, cycloalkyl and aralkyl groups are optionally substituted with one to five halogen;

R^2 is selected from C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, or aralkyl; wherein said alkyl, cycloalkyl, and aralkyl groups are optionally substituted with one to five halogen;

or a pharmaceutically acceptable salt or stereoisomer thereof.

18. A compound which is



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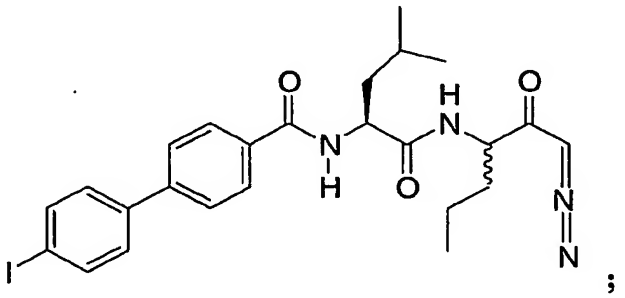
or a pharmaceutically acceptable salt or stereoisomer thereof.

19. A compound which is



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or a pharmaceutically acceptable salt or stereoisomer thereof.